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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 11/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,828	CREECH ET AL.	
	Examiner	Art Unit	
	Jon M Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *10-17 and 20-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-35* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *25 June 2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, Claims 1-9 and 18-19, as they are drawn to polynucleotides of SEQ ID NO:2 and SEQ ID NO:3, vectors, host cells, and methods of producing the polypeptide of SEQ ID NO:1, in the reply filed on 16 August 2004 is acknowledged. The traversal is on the ground(s) that the other Groups stem from a common concept and theory, and additional examination of Groups II-VIII would not place a substantially greater burden on the Examiner. This is not found persuasive because consistent with current Office practice, a serious search burden may be established by (A) separate classification, (B) separate status in the art when they are classifiable together, and (C) a different field of search. These criteria were met for reasons set forth in the previous Office Action mailed 21 June 2004. As stated in the MPEP § 803, "a serious burden on the Examiner may be *prima facie* shown if the Examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search defined in MPEP § 808.02". Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. Thus, the Groups require divergent searches, and to search all the inventions would be burdensome.

2. The requirement is still deemed proper and is therefore made FINAL.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(e), which papers have been placed of record in the file.

Information Disclosure Statement

4. The information disclosure statement (IDS), filed 25 June 2001, has been considered by the examiner.

Drawings

5. Applicants are advised that upon issuance of a patent, the complete text of the sequence listing submitted in compliance with 37 C.F.R.§§1.821-1.825 will be published as part of the patent. Therefore, it is unnecessarily redundant to repeat the sequence information in the form of Figures. Applicants should amend the specification to delete any Figures (e.g. Figures 2-4) which consist only of nucleic acid or protein sequences which have been submitted in their entirety in computer readable format (i.e. as SEQ ID NO:'s) and should further amend the specification accordingly to reflect the replacement of the Figure by the appropriate SEQ ID NO:.

Specification

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 21, line 22 and page 45, line 21, for example). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 101 and 35 USC §112

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
>
> The following is a quotation of the first paragraph of 35 U.S.C. 112:
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-9 and 18-19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility.

9. Claims 1-9 and 18-19 are drawn to a putative subunit of a cyclic nucleotide gated cation channel, human CNG3B protein (SEQ ID NO:1), the nucleic acids encoding the protein (SEQ ID NO:2 and SEQ ID NO:3) and a method of producing the protein. The claimed invention is not supported by either a specific and substantial asserted utility, or a well-established utility. A specific and substantial utility is one that is particular to the claimed subject matter and that identifies a "real world" context of use for the claimed invention which does not require further research.

10. The instant application discloses polynucleotide sequences set forth as SEQ ID NO:2 and SEQ ID NO:3 encoding a polypeptide as set forth as SEQ ID NO:1. The specification asserts that the instant application relates to a novel subunit of a cyclic nucleotide-gated ion channel

(CNG3B) (See page 4, lines 5-6) which is based upon sequence homology of the predicted amino acid sequence of the claimed CNG3B protein with previously cloned cyclic nucleotide-gated channels human alpha subunits CNGA1 and CNGA3 and a mouse beta subunit CNG6 (See page 63, line 30 – page 64, line 3). The specification further discloses that since CNG3B is similar to members of this family that are beta subunits [beta subunits of cyclic nucleotide gated ion channels], it is "most likely a beta subunit itself" (See page 8, lines 26-27). The instant specification fails to provide any experimental data or information on whether the CNG3B protein encoded by the claimed nucleic acids set forth as SEQ ID NO:2 or SEQ ID NO:3, functions like a cyclic nucleotide-gated ion channel, and determination/confirmation of the biological functions or activities of the claimed CNG3B protein would require undue experimentation. There is no well-established utility for a specific nucleic acid or amino acid sequence, and the specification fails to disclose a specific and substantial utility for the claimed invention. There are no working examples.

11. The instant specification asserts that the CNG3B protein can be used as a reporter molecule in assay and detection systems, to measure, for example, changes in cation concentration, membrane potential, or current flow, ion flux, transcription, signal transduction, receptor-ligand interactions, second messenger concentrations (See page 9, lines 7-16). The specification also asserts that the claimed invention provides for a method of screening mutations of CNG3B genes or proteins (See page 9, lines 21-28). However, such uses are all considered research uses only and are designed to identify a particular function of the claimed molecules and are not a substantial utility.

12. The specification further asserts that the claimed invention provides methods of screening for modulators, activators, and inhibitors of the CNG3B protein, and such modulators would be useful in the treatment of visual disorders, infertility, or useful as contraceptives (See page 8, line 30 – page 9, line 6). The specification further asserts that detection f CNG3B nucleic acid and protein expression allows diagnosis of visual disorders and male infertility (See page 9, lines 17-20). These asserted utilities are not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. The specification neither identifies the biological functions of the claimed proteins nor any disorders that are associated with the claimed molecules. Clearly, further research would be required to determine the functions of the claimed molecules or to identify a disease that can be treated or diagnosed with the claimed molecules.

13. The invention also lacks a well-established utility. A well established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. Novel biological molecules lack an established utility and must undergo extensive experimentation to determine an appropriate specific, substantial, and credible utility. The homology of the predicted amino acid sequence of the claimed CNG3B protein with known cyclic nucleotide-gated subunits does not endow the claimed molecules with a specific and substantial utility. Further, the CNG3B polypeptide set forth in SEQ ID NO:1 which is encoded by disclosed nucleic acids set forth as SEQ ID NO:2 or SEQ ID NO:3 has been deduced from the nucleic acid sequence (See page 63, lines 30-32) and has never been expressed in a cell or organism or assayed for functional activity. The diversity of the structure and functions of the cyclic nucleotide-gated ion channels (See Finn et al., 1996,

Annual Review of Physiology 58:395-426), is only complicated by the observation that function cannot be predicted based solely on structural similarity to a protein found in the sequence database. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (See Box 2, page 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (See especially page 399). Furthermore, no art of record discloses or suggests any property or activity for the claimed molecules such that another non-asserted utility would be well established for the compounds. Since the instant specification does not disclose how to use the polypeptide of SEQ ID NO:1, a skilled artisan would not know how to use the nucleic acids encoding the polypeptide (SEQ ID NO:2 and SEQ ID NO:3) without undue experimentation.

14. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct., 1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a nucleic acid that encodes a protein which has

undetermined function or biological significance. Until some actual and specific activity or significance can be attributed to the protein identified in the specification as SEQ ID NO:1 or the polynucleotide encoding it (SEQ ID NO:2 and SEQ ID NO:3), the claimed invention is incomplete.

15. Claims 1-9 and 18-19 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to make/use the claimed invention.

16. Furthermore, even if the nucleic acid molecules of SEQ ID NOs:2 and 3, or the amino acid encoded by them (SEQ ID NO:1) were to have a patentable utility, the instant disclosure would not be found to be enabling for the full scope of the claimed invention.

17. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

18. Claims 1, 2, 5, and 7-9 are drawn to a genus of nucleic acid molecules encoding a polypeptide comprising an amino acid sequence having at least 85% sequence identity to residues 210-661 of SEQ ID NO:1, comprising a nucleotide sequence that is amplified by

primers that hybridize under stringent conditions to the same sequence as the primers selected from the group consisting of SEQ ID NO:4-12, comprising a nucleotide sequence that hybridizes under stringent conditions to a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3, or comprising a nucleotide sequence that hybridizes under moderately stringent conditions to a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3. Claims 19-20 depend on claim 1. However, other than the protein of SEQ ID NO:1 and the DNA molecules of SEQ ID NO:2 and SEQ ID NO:3 that encode the protein, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. The disclosure has not shown (1) which portions of SEQ ID NO:2 or SEQ ID NO:3 are critical to the activity of the CNG3B polypeptide of SEQ ID NO:1 (which is itself unknown); (2) what modifications (e.g., substitutions, deletions, or additions) one can make to SEQ ID NO:2 or SEQ ID NO:3 that will result in protein mutants or variants with the same function/activity as the claimed CNG3B protein of SEQ ID NO:1; and (3) any guidance on how to use mutants or variants of SEQ ID NO:1 which would, based on the language of said claims, encompass both active and inactive variants of SEQ ID NO:1, or the nucleic acids that encode the aforementioned peptides. The state of the art is such that the relationship between the sequence of a protein and its activity is not well understood and unpredictable, and that certain positions in the sequence are critical to the protein's structure/function relationship and can only tolerate only relatively conservative substitutions or no substitutions (See Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., The Protein Folding Problem and Tertiary Structure Prediction, 1994, pp. 492-495).

19. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of substitutions/deletions on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

20. Claims 1, 2, 5, 7-9, and 19-20 are also rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was files, had possession of the claimed invention.

21. The specification discloses two nucleotide sequence set forth as SEQ ID NO:2 and SEQ ID NO:3, which encode a polypeptide of SEQ ID NO:1. However, claims 1, 2, 5, and 7-9, as written, recite a genus of nucleic acid molecules encoding a polypeptide comprising an amino acid sequence having at least 85% sequence identity to residues 210-661 of SEQ ID NO:1, comprising a nucleotide sequence that is amplified by primers that hybridize under stringent conditions to the same sequence as the primers selected from the group consisting of SEQ ID NO:4-12, comprising a nucleotide sequence that hybridizes under stringent conditions to a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3, or comprising a nucleotide sequence that hybridizes under moderately stringent conditions to a nucleic acid

comprising a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3. Thus, the claims encompass a large number of nucleic acids that vary substantially, both in length and in nucleotide composition.

22. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity. Furthermore, the only factor present in claims 5 and 7-9 is a mere chemical property of the DNA in the form of a recitation of hybridizes to the polynucleotide of SEQ ID NO:2 or SEQ ID NO:3, or the polynucleotide encoding the protein of SEQ ID NO:1. The specification does not identify any particular portion of the structure that must be conserved, nor does it provided any disclosure of a particular structure/function correlation or biological activity. The distinguishing characteristics of the claimed genus are not described. The only adequately described species are the polynucleotides represented by SEQ ID NO:2 and SEQ ID NO:3 that encode the CNG3B polypeptide of SEQ ID NO:1. Accordingly, the specification does not provide adequate written description of the claimed genus.

23. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

24. With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides and DNA molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

25. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

26. Therefore, only the polynucleotide that encodes the CNG3B polypeptide of SEQ ID NO:1 and the DNA molecules of SEQ ID NO:2 and SEQ ID NO:3, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, 2nd paragraph

27. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

28. Claims 1-9 and 18-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

29. Claims 1 and 8 are indefinite because it recites the abbreviation CNG3B, which should be spelled out in all independent claims in the interest of clarity. The mere recitation of an acronym is insufficient to indicate the metes and bounds of the claim. Moreover, since CNG3B refers to CNG3B polymorphic variants, alleles, mutants, and homologues (See page 10, line 19 – page 11, line 15), it is suggested that the term be spelled out at its first use and identified by sufficient structural and/or functional language to overcome this rejection.

29. Claim 1 is further indefinite because it is unclear what is meant by the phrase "forming, with at least one additional alpha subunit". As the claim does not previously refer to any alpha subunit, it is not clear what an "additional alpha subunit" might be.

30. Claim 7 is indefinite for reciting "specifically hybridizes under moderately stringent conditions". The specification discloses that "specifically hybridizes" refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent conditions (See page 22, lines 29-32).

Summary

39. No claim is allowed.

40. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

41. Gerstner et al. (15 February 2000). Molecular cloning and functional characterization of a new modulatory cyclic nucleotide-gated channel subunit from mouse retina. The Journal of Neuroscience 20(4):1324-1332. Gerstner et al teach a nucleic acid that encodes a protein that shares 81.8% identity to amino acids 210-661 of SEQ ID NO:1 of the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback, Ph.D.** can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
October 27, 2004

LORRAINE SPECTOR
PRIMARY EXAMINER